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| 10/659,200 | 09/10/2003 | Lorraine Grace Robb | 12768Z | 5578 |

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EXAMINER

BORGEEST, CHRISTINA M

ART UNIT PAPER NUMBER

1649

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|---------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/659,200 | Applicant(s) ROBB ET AL. | |
| | Examiner Christina Borgeest | Art Unit 1649 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-27 is/are pending in the application.
- 4a) Of the above claim(s) 27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>9/10/03; 5/6/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 25 and 26 in the reply filed on 9 May 2006 is acknowledged. The traversal is on the ground(s) that the examiner's authority to require restriction is limited to inventions that are both independent and distinct and that Groups I and II represent different aspects of a single invention linked by a single inventive concept. Furthermore, Applicants argue at p. 4 (entire page) that the classification system is a poor basis for requiring restriction. At p. 5-6 Applicants discuss the consequences of improper restriction to which the examiner takes no issue. These arguments are not found persuasive for the following reasons. First, with regard to the requirement for showing both independence and distinctness of inventions; see the MPEP 803 [R-3]:

Under the statute, the claims of an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP §802.01, §806.06, **and** §808.01) **or** distinct (MPEP §806.05 §806.05(j)) (emphasis added).

Thus the interpretation in the MPEP supports restriction made between inventions that are independent **or** distinct. Claims 25 and 26 (Group I) are drawn to protein therapy and claim 27 (Group II) is drawn to gene therapy, and within the Office these subjects are examined by examiners in different departments, called art units. Furthermore, gene therapy and protein therapy can support separate patents. Quality examination is the goal of the Office, and to ensure quality of examination, patent

applications are sent to art units staffed by examiners with the appropriate technical background. With regard to the classification system being a poor basis for restriction, examination of applications requires not just a search in the patent and non-patent literature, but a consideration of enablement and written description issues that are best made by examiners with the appropriate technical background. In addition, with regard to search burden, protein therapy art would not anticipate nor render obvious gene therapy art, and thus a much broader search would have to be conducted to examine both in the same application. If Applicants would like to make a statement on the record admitting that protein therapy art would render obvious or anticipate gene therapy art, the Office can examine the two independent Groups together.

The requirement is still deemed proper and is therefore made FINAL.

Claim 27 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention (gene therapy), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9 May 2006.

Claims 25 and 26 are pending and under consideration.

Information Disclosure Statement

The information disclosure statement filed 3 September 2004 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance of the Japanese language abstract (citation 13), as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the

information. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is drawn to “[a] method for enhancing decidualization and fertility in an animal...”, and the meaning of deciduas is the mucous membrane lining of the uterus (see definition in Answers.com, accessed 27 June 2006 at answers.com/topic/decidua. During decidualization the lining becomes thicker and evolves during pregnancy. The claim, which recites “animal,” is not limited to females, and since males do not have a decidual lining, claim 25 is indefinite because it is not clear what Applicants intend to claim.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims require the co-administration of IL-11 and IL-11R α , however, the specification as filed never contemplated the administration of the combination of these agents. Furthermore, the specification as originally filed does not contemplate administering IL-11R α . The original specification discloses decreasing fertility by applying ***antagonists of IL-11-IL-11R α interaction***, however, nowhere is the co-administration of IL-11 and IL-11R α contemplated.

Claim 26 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing fertility by administering an effective amount of IL-11 and IL-11R α , does not reasonably provide enablement for a method of administering functional derivatives of IL-11 and IL-11R α . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors

include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claim is broad; claim (26) recites “functional derivatives” of IL-11 and IL-11R α , which amounts to a single means claim. Single means claims are those that cover every conceivable means for achieving the stated purpose. Single means claims are nonenabling for the scope of the claim because the specification discloses at most only those means known to the inventor, in this case, IL-11 or IL-11R α . When claims depend on a recited property, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See MPEP 2164.08(a). “Derivatives” encompass those agents that are undiscovered as well as discovered for the purpose of agonizing the interaction between IL-11 and IL-11R α , thus there are no metes and bounds to limit the claim for the purpose of establishing patent rights and infringement.

The nature of the invention is complex; protein therapy is fraught with problems, not least of all expense, short half life, vulnerability to proteolytic degradation, and undesired pleiotropic effects (see Saragovi & Burgess, *Exp Opin Ther Patents*. 1999; 9: 737-751, p. 739, left column, 2nd paragraph). Furthermore, the use of IL-11R α as a therapeutic is a relatively underpublished area. A search in MEDLINE for the use of IL-

IL-11R α as a therapeutic turns up only a handful of articles, most of which are related to the use of IL-11 as a therapeutic, thus the art is unpredictable at this state of development. Furthermore, in the absence of the teachings in the prior art, the specification should provide guidance, and with regard to "derivatives" of IL-11 and IL-11R α , it provides neither detailed guidance nor any working examples.

Due to the large quantity of experimentation necessary to test for all possible derivatives of IL-11 and IL-11R α that are capable of agonizing the interaction between IL-11 and IL-11R α , the lack of direction/guidance presented in the specification regarding and the absence of working examples directed to the same, the complex nature of the invention, the relatively nascent state of the prior art with regard to therapeutic use of IL-11R α , and the breadth of the claims which fail to recite limitations on "derivatives" of IL-11 and IL-11R α , undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

In addition, claim 26 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of a “functional derivative” of IL-11 and IL-11R α . There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

With the exception of administration of IL-11 and IL-11R α , the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only administration of IL-11 and IL-11R α , but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith (WO 95/24650—reference 1 on Applicants' 1449 form filed 6 May 2004) in view of Ireland et al. (Meeting abstract, 1994—reference 6 on Applicants' 1449 form, filed 6 May 2004) and further in view of Karow et al. (Biochem J. 1996, 318; 489-495—reference 8 on Applicants' 1449 form filed 6 May 2004). Keith teaches the administration of IL-11 to women for the purpose of treatment of gestational diabetes and hypertension (see, for instance, p. 3, 1st and 2nd paragraphs; p. 6, 2nd paragraph; p. 7, 2nd paragraph). Keith does not teach the co-administration of IL-11R α , nor does he teach the administration of IL-11 and IL-11R α for the purpose of enhancing decidualization or fertility or in an amount effective to agonize the interaction between IL-11 and IL-11R α . Ireland et al. suggest that IL-11 may have an important role in trophoblast differentiation and placental implantation and maintenance of pregnancy (see whole document), all of which speak to enhancement of fertility. While Ireland et al. do not specifically use the term “decidualization”, they describe IL-11 as being important for the maintenance of the early stages of pregnancy, of which decidualization is an important part. It is obvious in the art that the very early stages of pregnancy, implantation and invasion into the decidua and decidualization are integrated and interdependent processes that are not separable from one another. Finally, Karow et al. teach that a soluble form of IL-11, IL-11R α , when co-administered with IL-11 is able to potentiate IL-11 bioactivity (see p. 493, right column, last paragraph, and Figure 4b). In addition, Karow et al. teach at p. 494, left column, 4th paragraph that at the amounts they administered:

[A] complex of IL-11 and [soluble]IL-11R is able to interact with gp130 with high affinity. The high affinity interaction with IL-11r is therefore the principle determinant of ligand specificity in the formation of the active signaling complex. This also suggests that the formation of a high-affinity complex involves IL-11R mediated conformational changes in the IL-11 ligand and/or direct interaction between binding sites on gp130 and the IL-11R.

In other words, the amount was effective in agonizing the interaction between IL-11 and IL-11R α . It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Keith by using the invention to enhance fertility via supporting early pregnancy, as taught in Ireland and to co-administer IL-11R α as taught by Karow et al. for several reasons. First, although Keith does not specifically teach administering IL-11 to support early pregnancy, he does teach the administration of IL-11 to pregnant women, so the patient population overlaps. Second, Ireland et al. suggest that IL-11 may have an important role in early pregnancy support, thus it is an obvious modification to administer IL-11 at the start early stages of pregnancy. Third, it would have been obvious to co-administer IL-11R α because, according to Karow et al., "the soluble form of IL-11R is able to mediate IL-11 dependent responses" (see p. 494, left column, 4th paragraph) and that "the evidence...indicates that the characteristic biological effects of IL-11 are controlled in vivo by the tissue specific expression and bioavailability of the cognate receptors," (see p. 494, right column, 2nd paragraph). The person of ordinary skill in the art would have been motivated to modify the teachings of Keith by co-administering IL-11R α to women to support the early stages of pregnancy because the teachings of Ireland et al. suggest the importance of IL-11 in the support of early pregnancy and the teachings of Karow et

Art Unit: 1649

al. suggest the ability of IL-11R α to potentiate IL-11 bioactivity, which may be important in a case where IL-11 is administered but does not elicit an appropriate biological response. Furthermore, the person of ordinary skill in the art could have reasonably expected success because of the success of the experiments as reported by Ireland et al. and Karow et al. Thus the claims do not contribute anything non-obvious over the prior art.

Conclusion

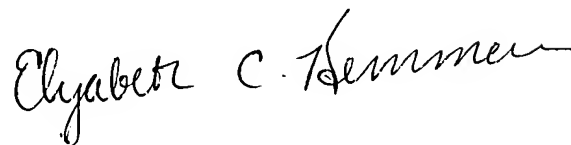
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest, Ph.D.



ELIZABETH KEMMERER
PRIMARY EXAMINER